

Amendments to the Claims:

Please, **cancel** pending claims 1-17, 27, 30-34 and 40-43 without prejudice.

Please, **add** new claims 44 - 88 as follows:

**44.** A synthetic protein comprising a retroinverted peptide, said retroinverted peptide being the retro-inverted form of an L-peptide that has an amino acid sequence selected from the group consisting of SEQ ID NOS: **16-70**; said synthetic protein being one that specifically binds to a Caco-2 cell membrane fraction.

**45.** A synthetic protein of claim 44 wherein the protein consists of not more than 75 amino acids.

**46.** A synthetic protein of Claims 44 wherein the protein is the retroinverted peptide.

**47.** A synthetic protein comprising either a retro-inverted peptide or fragment thereof, said retroinverted peptide being the retroinverted form of an L-peptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NOS: **16-70**, wherein said fragment has at least five contiguous amino acids and wherein said synthetic protein specifically binds to a Caco-2 cell membrane fraction.

**48.** A synthetic protein of Claim 47 wherein the fragment has at least 10 contiguous amino acids.

**49.** A synthetic protein of Claim 48 wherein the fragment has at least 20 contiguous amino acids.

**50.** A synthetic protein of claim 47, wherein the fragment consists of an amino acid sequence selected from the group consisting of:

- (a) rtrlrrnhsshkant (SEQ ID NO:1), which is the retro-inverted form of the L-peptide TNAKHSSHNRRLRTR (SEQ ID NO:4);
- (b) gphrrgrpnsrsskrt (SEQ ID NO:2), which is the retro-inverted form of the L-peptide TRKSSRSNPRGRRHPG (SEQ ID NO:5); and
- (c) gtsngngccnydgp (SEQ ID NO:3), which is the retro-inverted form of the L-peptide PGDYNCCGNGNSTG (SEQ ID NO:6).

**51.** A synthetic protein of Claim 50 wherein the synthetic protein is a fragment consisting of an amino acid sequence selected from the group consisting of:

- (a) rtrlrrnhsshkant (SEQ ID NO:1), which is the retro-inverted form of the L-peptide TNAKHSSHNRRLRTR (SEQ ID NO:4);
- (b) gphrrgrpnsrsskrt (SEQ ID NO:2), which is the retro-inverted form of the L-peptide TRKSSRSNPRGRRHPG (SEQ ID NO:5); and
- (c) gtsngngccnydgp (SEQ ID NO:3), which is the retro-inverted form of the L-peptide PGDYNCCGNGNSTG (SEQ ID NO:6).

**52.** A synthetic protein of claims 47-50 wherein the synthetic protein consists of not more than 75 amino acids.

**53.** A synthetic protein of claims 47-50 wherein the synthetic protein consists of not more than 50 amino acids.

**54.** A synthetic protein comprising either a retro-inverted peptide or a homolog of said retro-inverted peptide, said retroinverted peptide being the retroinverted form of an L-peptide that consisting of an amino acid sequence selected from the group consisting of SEQ ID NOS: **16-70**,

wherein said homolog is based on percent homology or on amino acid functional equivalency,

wherein said synthetic protein specifically binds to a Caco-2 cell membrane fraction,  
wherein a homolog based on percent homology is one that has at least 80 % but  
less than 100% identity with said retro-inverted peptide when the homolog is compared to  
a sequence of equal length of the retroinverted peptide, and

wherein a homolog based on amino acid functional equivalency is one that  
comprises one or more amino acid differences compared to the retroinverted peptide, and  
wherein each amino acid difference is consistent with the following rules:

- 1) a nonpolar amino acid is replaced by another nonpolar amino acid, wherein  
the nonpolar amino acids are alanine, leucine, isoleucine, valine, proline, phenylalanine,  
tryptophan and methionine;
- 2) a polar neutral amino acid is replaced by another polar neutral amino acid  
wherein the polar neutral amino acids are glycine, serine, threonine, cysteine, tyrosine,  
asparagine, and glutamine;
- 3) a positively charged amino acid is replaced by another positively charged  
amino acid wherein the positively charged amino acids are arginine, lysine, and histidine;  
and
- 4) a negatively charged amino acid is replaced by another negatively charged  
amino acid, wherein the negatively charged amino acids are aspartic acid and glutamic  
acid.

55. A synthetic protein of claim 54 wherein the homolog is based on percent  
homology.

56. A synthetic protein of Claim 55 wherein the homolog has at least 90 % but  
less than 100% identity with said retro-inverted peptide when the homolog is compared to  
a sequence of equal length of the retroinverted peptide.

57. A synthetic protein of Claim 54 wherein the homolog is based on amino acid functional equivalency.

58. A synthetic protein comprising either a retro-inverted peptide, a fragment of at least five contiguous amino acids of said retroinverted peptide, or a homolog of said fragment,

wherein said retroinverted peptide is the retroinverted form of an L-peptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NOS 16-70,

wherein said homolog is based on percent homology or on amino acid functional equivalency,

wherein said synthetic protein specifically binds to a Caco-2 cell membrane fraction; wherein said homolog has at least 80 % but less than 100% identity with said fragment when the homolog is compared to a sequence of equal length of the fragment, and

wherein a homolog based on amino acid functional equivalency is one that comprises one or more amino acid differences compared to the retroinverted peptide, and wherein each amino acid difference is consistent with the following rules:

- 1) a nonpolar amino acid is replaced by another nonpolar amino acid, wherein the nonpolar amino acids are alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine;
- 2) a polar neutral amino acid is replaced by another polar neutral amino acid wherein the polar neutral amino acids are glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine;

3) a positively charged amino acid is replaced by another positively charged amino acid wherein the positively charged amino acids are arginine, lysine, and histidine; and

4) a negatively charged amino acid is replaced by another negatively charged amino acid, wherein the negatively charged amino acids are aspartic acid and glutamic acid.

59. A synthetic protein of Claim 58 wherein the fragment has at least 10 contiguous amino acids.

60. A synthetic protein of Claim 59 wherein the fragment has at least 20 contiguous amino acids.

61. A synthetic protein of claim 58, wherein the fragment consists of an amino acid sequence selected from the group consisting of:

- (a) rtrIrrnhsshkant (SEQ ID NO:1), which is the retro-inverted form of the L-peptide TNAKHSSHNRRLRTR (SEQ ID NO:4);
- (b) gphrrgrpnsrsskrt (SEQ ID NO:2), which is the retro-inverted form of the L-peptide TRKSSRSNPRGRRHPG (SEQ ID NO:5); and
- (c) gtsngngccnydgp (SEQ ID NO:3), which is the retro-inverted form of the L-peptide PGDYNCCGNGNSTG (SEQ ID NO:6).

62. A synthetic protein of Claim 61 wherein the synthetic protein is a fragment consisting of an amino acid sequence selected from the group consisting of:

- (a) rtrIrrnhsshkant (SEQ ID NO:1), which is the retro-inverted form of the L-peptide TNAKHSSHNRRLRTR (SEQ ID NO:4);

- (b) gphrrgrpnsrsskrt (SEQ ID NO:2), which is the retro-inverted form of the L-peptide TRKSSRSNPRGRRHPG (SEQ ID NO:5); and
- (c) gtsngngccnydgp (SEQ ID NO:3), which is the retro-inverted form of the L-peptide PGDYNCCGNGNSTG (SEQ ID NO:6).

63. A synthetic protein of claim 58 wherein the protein consists of not more than 75 amino acids.

64. A synthetic protein of claim 63 wherein the protein consists of not more than 50 amino acids.

65. A synthetic protein of claim 58 wherein the homolog is based on percent homology.

66. A synthetic protein of Claim 65 wherein the homolog has at least 90 % but less than 100% identity with said retro-inverted peptide when the homolog is compared to a sequence of equal length of the retroinverted peptide.

67. A synthetic protein of Claim 58 wherein the homolog is based on amino acid functional equivalency.

68. A synthetic protein of not more than 50 amino acids comprising a retroinverted peptide, such retroinverted peptide being the retroinverted form of an L-peptide consisting of an amino acid sequence selected from the group consisting of

- (a) Xaa<sub>1</sub> Thr Xaa<sub>2</sub> Xaa<sub>3</sub> Ser Xaa<sub>4</sub> Xaa<sub>5</sub> Xaa<sub>6</sub> Asn Xaa<sub>7</sub> Arg (SEQ ID NO: 71), where Xaa<sub>1</sub> is Ser or Thr; Xaa<sub>2</sub> is Arg or Lys; Xaa<sub>3</sub> is Lys or Arg; Xaa<sub>4</sub> is Ser or Leu; Xaa<sub>5</sub> is Arg, Ile, Val, or Ser; Xaa<sub>6</sub> is Ser, Tyr, Phe, or His; and Xaa<sub>7</sub> is Pro, His or Arg;
- (b) Asp Xaa<sub>1</sub> Asp Xaa<sub>2</sub> Arg Arg Xaa<sub>3</sub> Xaa<sub>4</sub> (SEQ ID NO: 72) where Xaa<sub>1</sub> is Ser, Ala, or Gly; Xaa<sub>2</sub> is Val or Gln; Xaa<sub>3</sub> is Pro, Gly, or Ser; and Xaa<sub>4</sub> is Trp or

Tyr;

- (c) Val Arg Ser Gly Cys Gly Xaa<sub>1</sub> Xaa<sub>2</sub> Ser Ser (SEQ ID NO: 73), where Xaa<sub>1</sub> is Ala or Phe; and Xaa<sub>2</sub> is Arg or His;
- (d) NTRKSSRSNPR (SEQ ID NO: 74);
- (e) STKRSLIYNHR (SEQ ID NO: 75);
- (f) STGRKVFNRR (SEQ ID NO: 76);
- (g) TNAKHSSHNR (SEQ ID NO: 77);
- (h) DSDVRRPW (SEQ ID NO: 78);
- (i) AADQRRGW (SEQ ID NO: 79);
- (j) DGRGGRSY (SEQ ID NO: 80);
- (k) RVRS (SEQ ID NO: 81);
- (l) SVRSGCGFRGSS (SEQ ID NO: 82);
- (m) SVRGGCGAHSS (SEQ ID NO: 83);

wherein said synthetic protein specifically binds to CaCo-2 cell membrane fraction.

**69.** The synthetic protein of claim 68 wherein the selected amino acid sequence is SEQ ID NO: 71.

**70.** The synthetic protein of claim 68 wherein the selected amino acid sequence is SEQ ID NO: 72.

**71.** The synthetic protein of claim 68 wherein the selected amino acid sequence is SEQ ID NO: 73.

**72.** The synthetic protein of claim 68 wherein the amino acid sequence is selected from the group consisting of SEQ ID NOS: 74-77.

**73.** The synthetic protein of claim 68 wherein the amino acid sequence is selected from the group consisting of SEQ ID NOS: 78-80.

74. The synthetic protein of claim 68 wherein the amino acid sequence is selected from the group consisting of SEQ ID NOS: 81-83.

75. A synthetic protein of claims 44, 47, 54, 58, or 68 wherein one or more amino acids of the retroinverted peptide, fragment, or homolog thereof, has undergone derivatization selected from the group consisting of glycosylation, acetylation, phosphorylation, amidation and

wherein said homolog that has undergone derivatization binds specifically binds to a Caco-2 cell membrane fraction.

76. A composition comprising the synthetic protein of Claims 44, 47, 54, 58, or 68, wherein the synthetic protein is coated onto or absorbed onto or covalently bonded to the surface of a nanoparticle or microparticle.

77. A composition of Claim 76 wherein the particle size of the nanoparticle or microparticle is between 10 nm and 500  $\mu$ m.

78. A composition of Claim 76 wherein the nanoparticle or microparticle is a drug-loaded or drug-encapsulating nanoparticle or microparticle.

79. A composition comprising both a synthetic protein of Claims 44, 47, 54, 58 or 68, and a material comprising a drug.

80. A composition of Claim 79 wherein the material is a slow-release device.

81. A composition of Claim 79 wherein the synthetic protein is covalently bound to the material.

82. A composition of Claim 79 wherein the synthetic protein is non-covalently bound to the material.

83. A composition of Claim 78 wherein the drug is selected from the group consisting of a peptide, a protein, a hormone, an analgesic, an anti-migraine agent, an anti-

coagulant agent, a cardiovascular agent, and anti-emetic agent, a narcotic antagonist, a chelating agent, an anti-anginal agent, a chemotherapeutic agent, a sedative, an anti-neoplastic agent, a prostoglandin, an antidiuretic agent, an anti-sense oligonucleotide, a gene, a gene- correcting hybrid oligonucleotide, a ribozyme, an aptameric oligonucleotide, a triple-helix forming oligonucleotide, a signal transduction pathway inhibitor, a tyrosine kinase inhibitor, a DNA-modifying agent, a non-viral gene delivery system, and a viral vector gene system.

**84.** A composition of Claim 78 wherein the drug is selected from the group consisting of insulin, calcitonin, calcitonin gene regulating protein, atrial natriuretic protein, colony stimulating factor, betaseron, erythropoietin,  $\alpha$ -interferon,  $\beta$ -interferon,  $\gamma$ -interferon, somatropin, somatotropin, somatotstatin, somatomedins, luteinizing hormone-releasing hormone, tissue plasminogen activator, growth hormone releasing hormone, oxytocin, estradiol, growth hormones, leuprolide acetate, factor VIII, interleukins, fentanyl, sufentanil, butorphanol, buprenophrine, levorphanol, morphine, hydromorphone, hydrocodone, oxymorphone, methadone, lidocaine, bupivacaine, diclofenac, naproxen, paverin, heparin, hirudin, scopolamine, ondansetron, domperidone, etoclopramide, diltiazem, clonidine, nifedipine, verapamil, isosorbide-5-mononitrate, benzodiazepines, phenothiazines, naltrexone, naloxone, deferoxamine, desmopressin, vasopressin, nitroglycerine, 5-fluorouracil, bleomycin, prostaglandins, and vincristine.

**85.** A composition of Claim 78 wherein the drug is insulin or leuprolide.

**86.** A composition of Claim 79 wherein the drug is selected from the group consisting of a peptide, a protein, a hormone, an analgesic, an anti-migraine agent, an anti-coagulant agent, a cardiovascular agent, and anti-emetic agent, a narcotic antagonist, a chelating agent, an anti-anginal agent, a chemotherapeutic agent, a sedative, an anti-

neoplastic agent, a prostoglandin, an antidiuretic agent, an anti-sense oligonucleotide, a gene, a gene- correcting hybrid oligonucleotide, a ribozyme, an aptameric oligonucleotide, a triple-helix forming oligonucleotide, a signal transduction pathway inhibitor, a tyrosine kinase inhibitor, a DNA-modifying agent, a non-viral gene delivery system, and a viral vector gene system.

87. A composition of Claim 79 wherein the drug is selected from the group consisting of insulin, calcitonin, calcitonin gene regulating protein, atrial natriuretic protein, colony stimulating factor, betaseron, erythropoietin,  $\alpha$ -interferon,  $\beta$ -interferon,  $\gamma$ -interferon, somatropin, somatotropin, somatotstatin, somatomedins, luteinizing hormone-releasing hormone, tissue plasminogen activator, growth hormone releasing hormone, oxytocin, estradiol, growth hormones, leuprolide acetate, factor VIII, interleukins, fentanyl, sufentanil, butorphanol, buprenorphine, levorphanol, morphine, hydromorphone, hydrocodone, oxymorphone, methadone, lidocaine, bupivacaine, diclofenac, naproxen, paverin, heparin, hirudin, scopolamine, ondansetron, domperidone, etoclopramide, diltiazem, clonidine, nifedipine, verapamil, isosorbide-5-mononitrate, benzodiazepines, phenothiazines, naltrexone, naloxone, deferoxamine, desmopressin, vasopressin, nitroglycerine, 5-fluorouracil, bleomycin, prostaglandins, and vincristine.

88. A composition of Claim 79 wherein the drug is insulin or leuprolide.